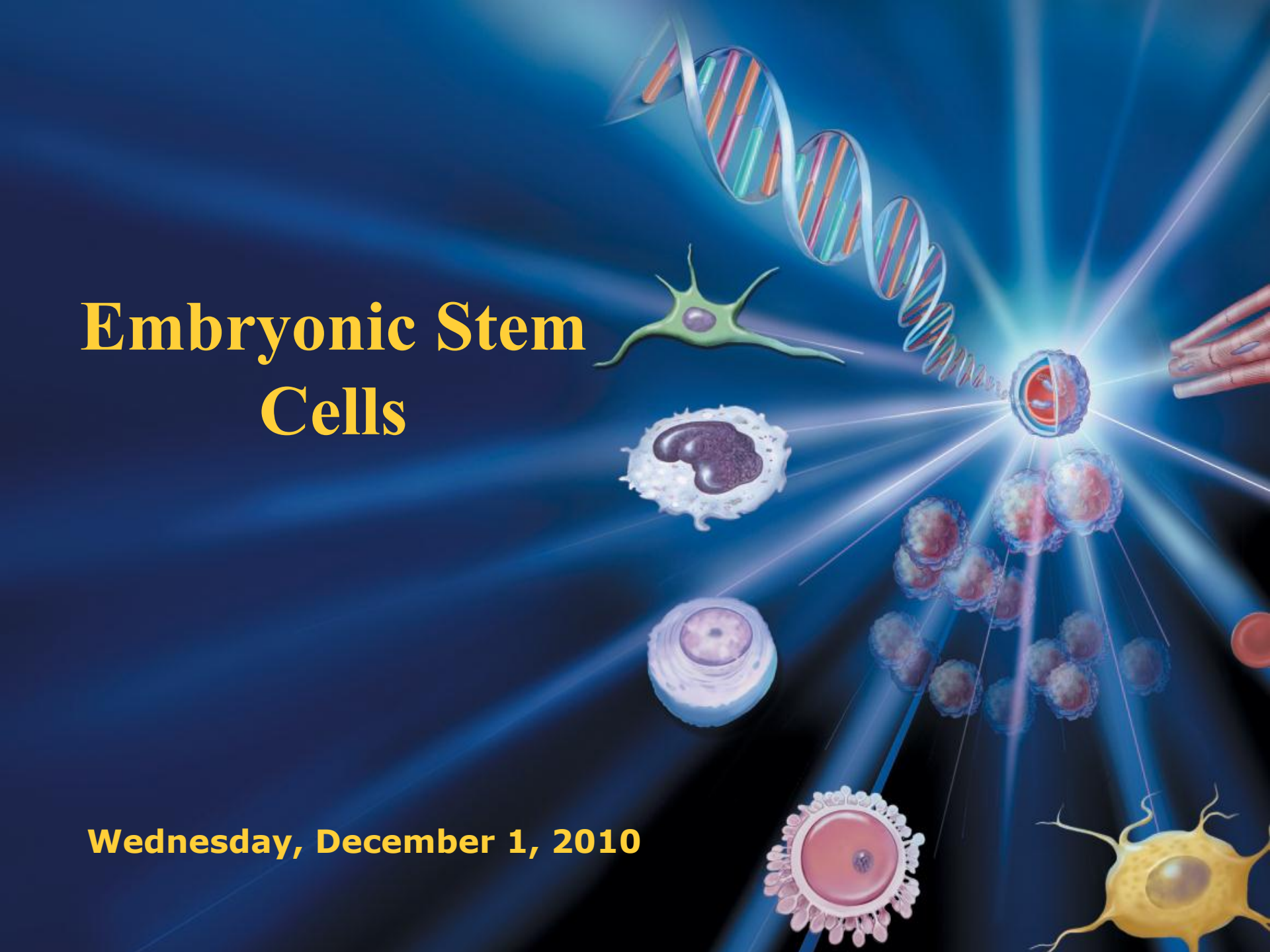
Embryonic Stem Cells



Wednesday, December 1, 2010

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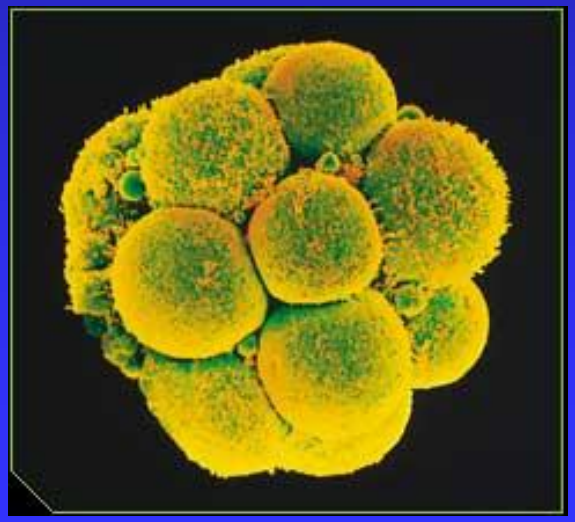
WITH STEM CELLS WE CAN GROW JUST ABOUT ANYTHING...
ETHICAL DILEMMA

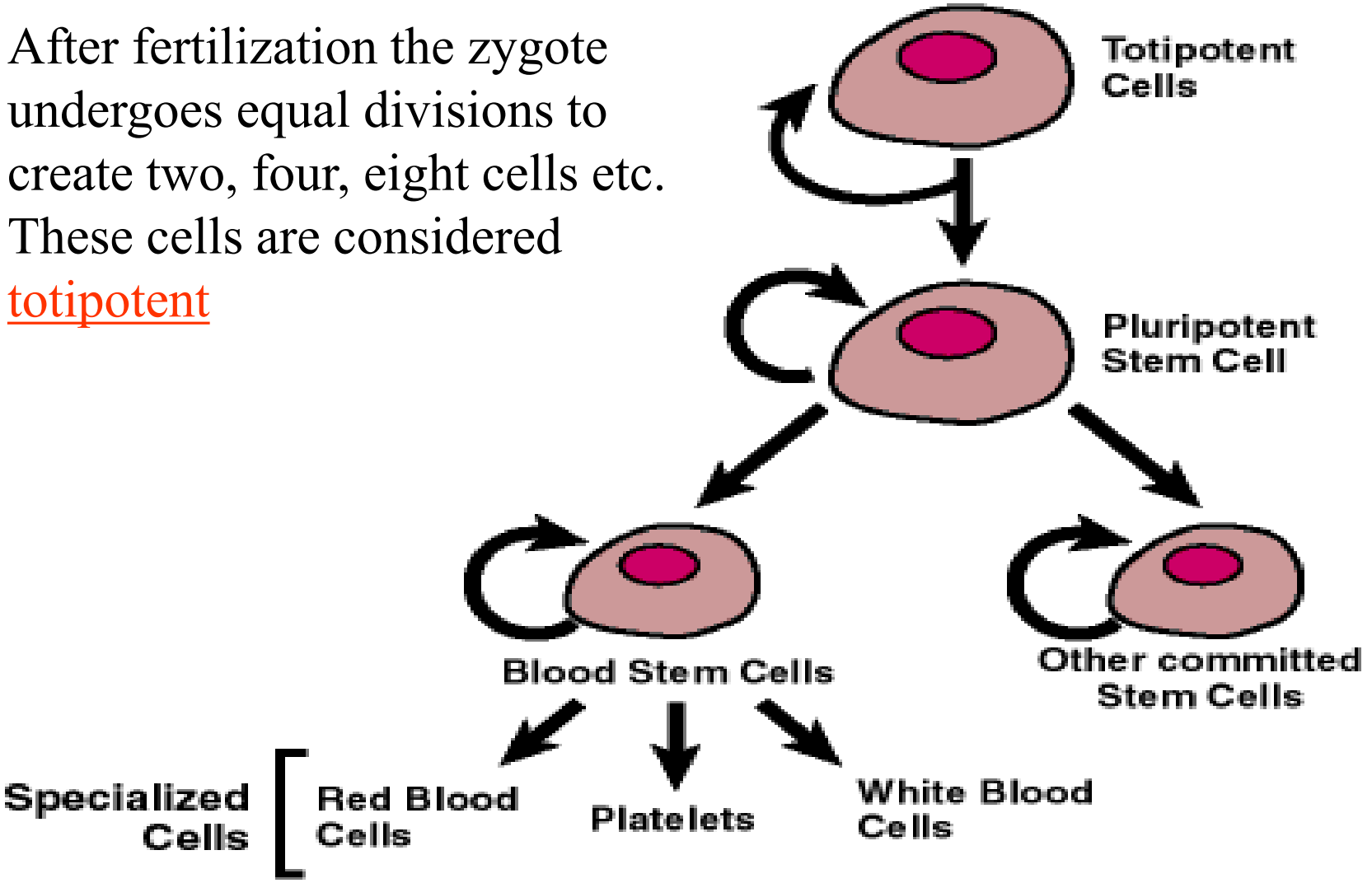
Stem Cells: What are they?

- **A cell that has the ability to continuously divide and differentiate (develop) into various other kind(s) of cells/tissues**
- **Cells that are developmentally "plastic": they can take different pathways and develop different cell types.**
- I.e. Heart cells, liver cells, skin cells, nerve cells etc.



Embryo three days after fertilization
(www.hhmi.org/bulletin/mar2002/stemcells/harvest.html)

After fertilization the zygote undergoes equal divisions to create two, four, eight cells etc. These cells are considered totipotent



Totipotent cells differentiate into pluripotent which will differentiate into Multipotent and then all types of tissues in the body

Types of Stem Cells

Stem cell type	Description	Examples
Totipotent	Each cell can develop into a new individual	Cells from early (1-3 days) embryos
Pluripotent	Cells can form any (over 200) cell types	Some cells of blastocyst (5 to 14 days)
Multipotent	Cells differentiated, but can form a number of other tissues	Fetal tissue, cord blood, and adult stem cells

What's So Special About Stem Cells?

- They have the potential to replace cell tissue that has been damaged or destroyed by severe illnesses.
- They can replicate themselves over and over for a very long time.
- Understanding how stem cells develop into healthy and diseased cells will assist the search for cures.

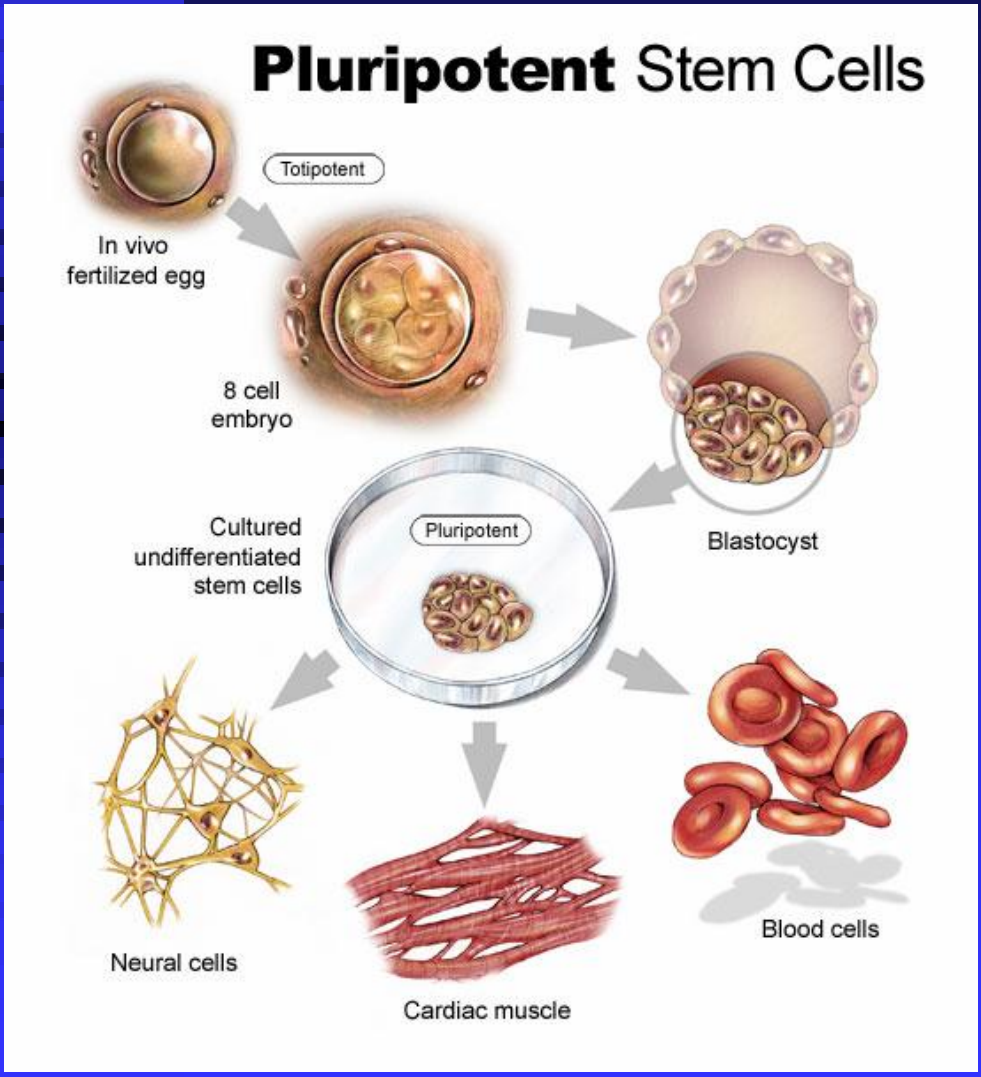
Sources of stem cells

- Adult Stem Cells
- Embryonic Stem Cells
- Embryonic Germ Cells
- Induced Pluripotent Stem Cells

Adult Stem Cells

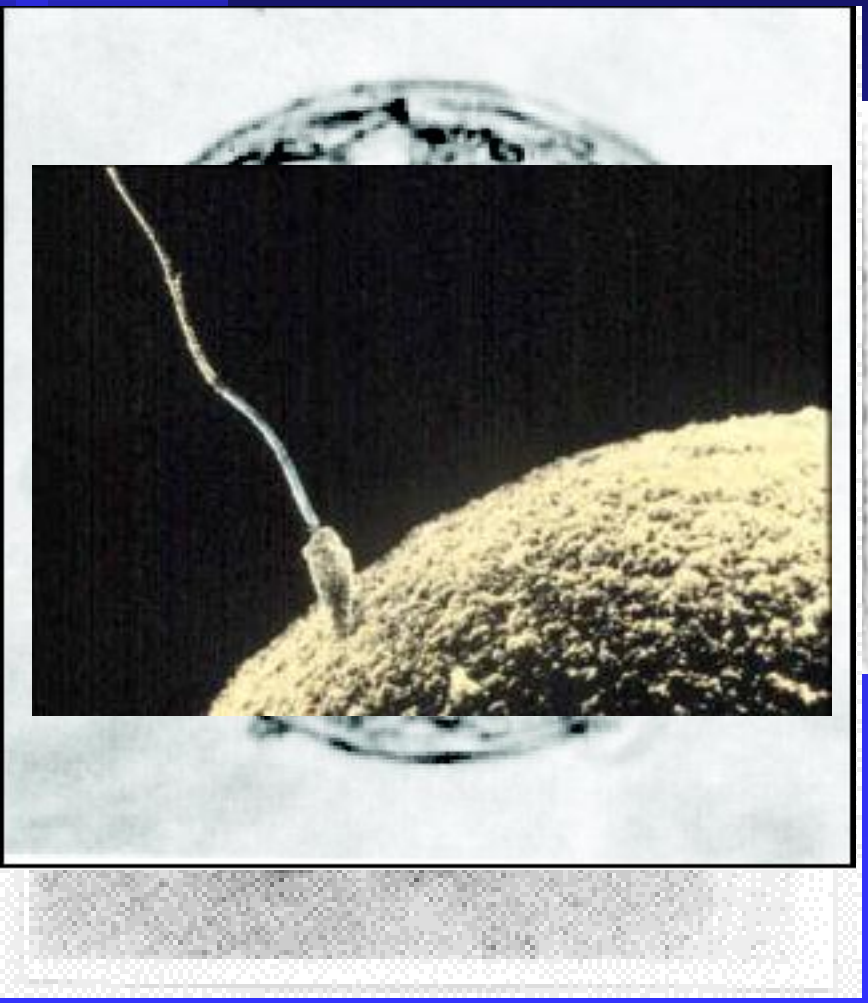
- Haven't been isolated for all tissue types
- Present in small quantities
- Difficulties in isolation and purification
- Numbers and quality decrease with age
- Differentiate into a narrower range of cell types

What about embryonic stem cells?



- They are undifferentiated cells that have the ability to form any adult cell.
- Undifferentiated embryonic stem cells can proliferate in culture. They can potentially provide adult cells such as bone, muscles, liver or blood cells.

Starting an embryonic stem cell line



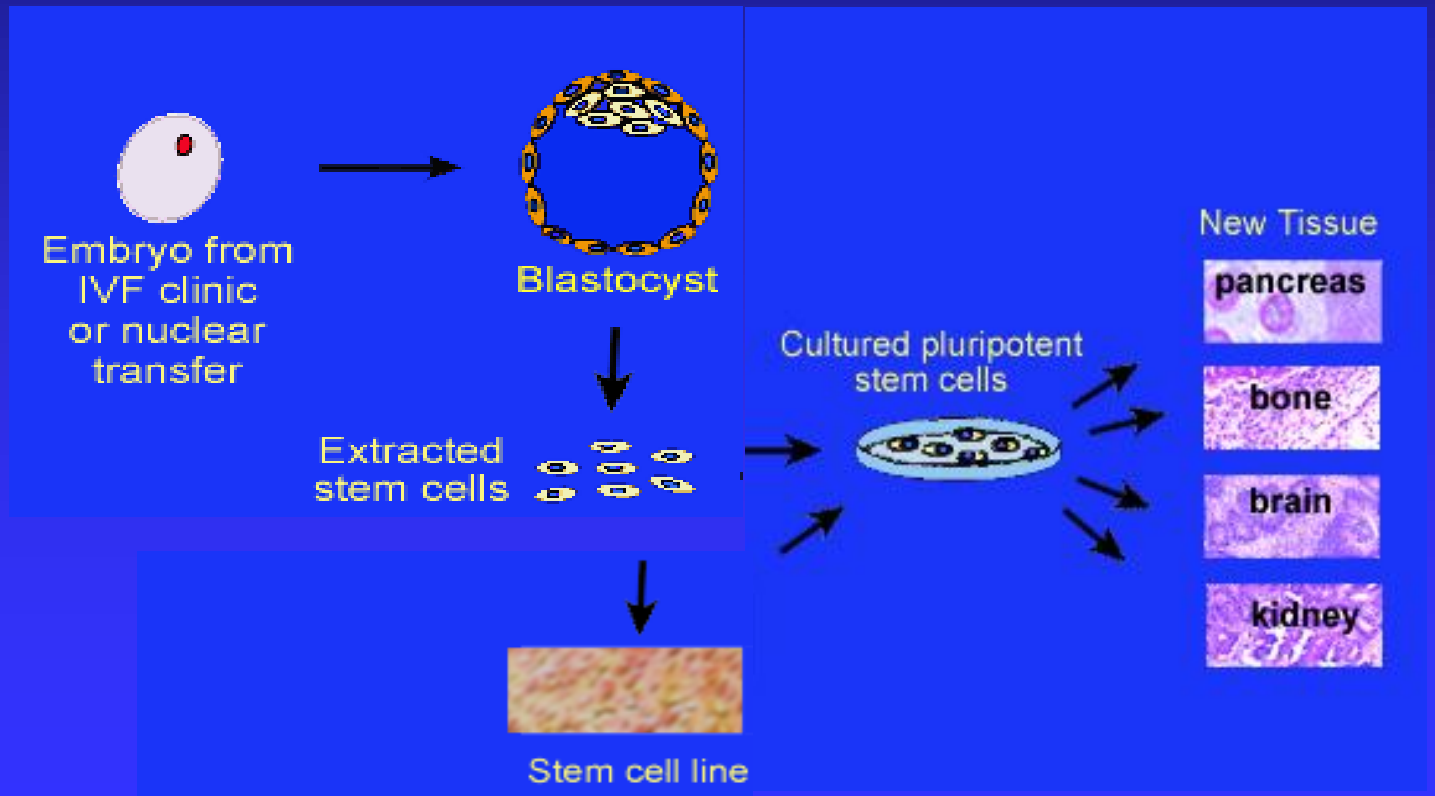
After fertilization the zygote undergoes equal divisions to create two, four, eight cells etc. These cells are totipotent Approximately four days after fertilization and several mitotic divisions the totipotent cells begin to forming a sphere of cells, called blastocyst. An outer layer develops which will become the placenta and other supporting tissues. An inner cell mass develops which will form every type of cell found in the human body. These cells are considered Pluripotent – they can give rise to many types of cells but not all types necessary for fetal development.

Embryonic Stem Cells:

Researchers extract stem cells from 5-7 days old blastocyst.

Stem cells can divide in culture to form more of their own kind, thereby creating a stem cell line.

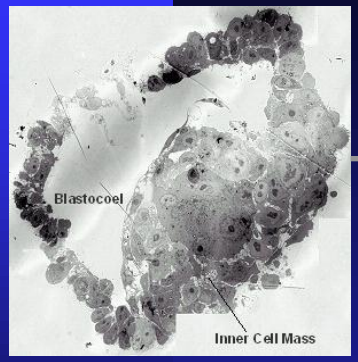
The research aims to induce these cells to generate healthy tissue needed by patients.



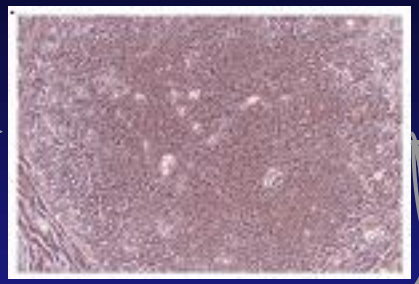
What are the embryonic germ layers?

- Stem cell can derived to from three embryonic germ layers:
- Endoderm (cartilage, bone, smooth muscle and striated muscle).
- Mesoderm (neural epithelium, embryonic ganglia).
- Ectoderm (stratified squamous epithelium).

Human Embryonic Stem Cells

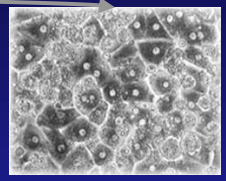


Blastocyst

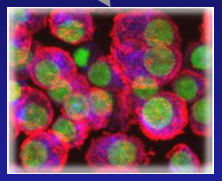


Human Embryonic Stem Cells

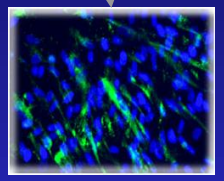
➡ Large Characterized cGMP Banks



Hepatocytes



Chondrocytes

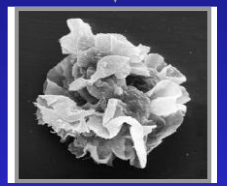


Osteoblasts

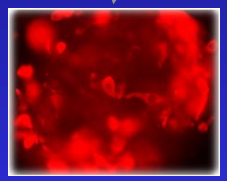
Drug Discovery
Liver Failure

Arthritis

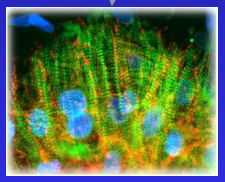
Osteoporosis
And Bone
Fractures



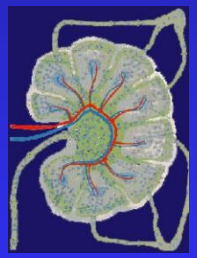
Dendritic Cells



Islets

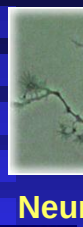


Cardiomyocytes



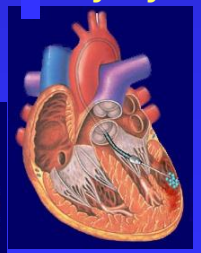
Tolerance Induction
Cancer Immunotherapy

Diabetes



Spinal Cord
Injury

Parkinson's
Disease



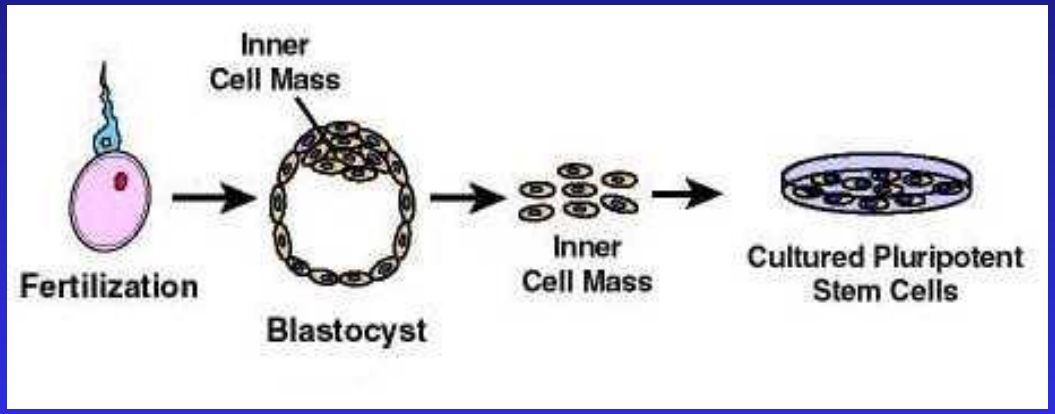
Heart Failure

Neural Cells

➡ Therapeutic Cells

Embryonic *vs* adult stem cells

- ES cells come from ICM of blastocyst



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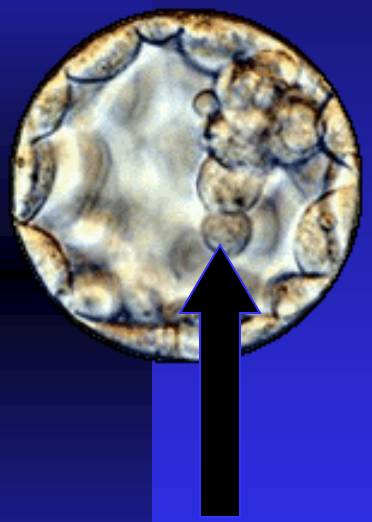
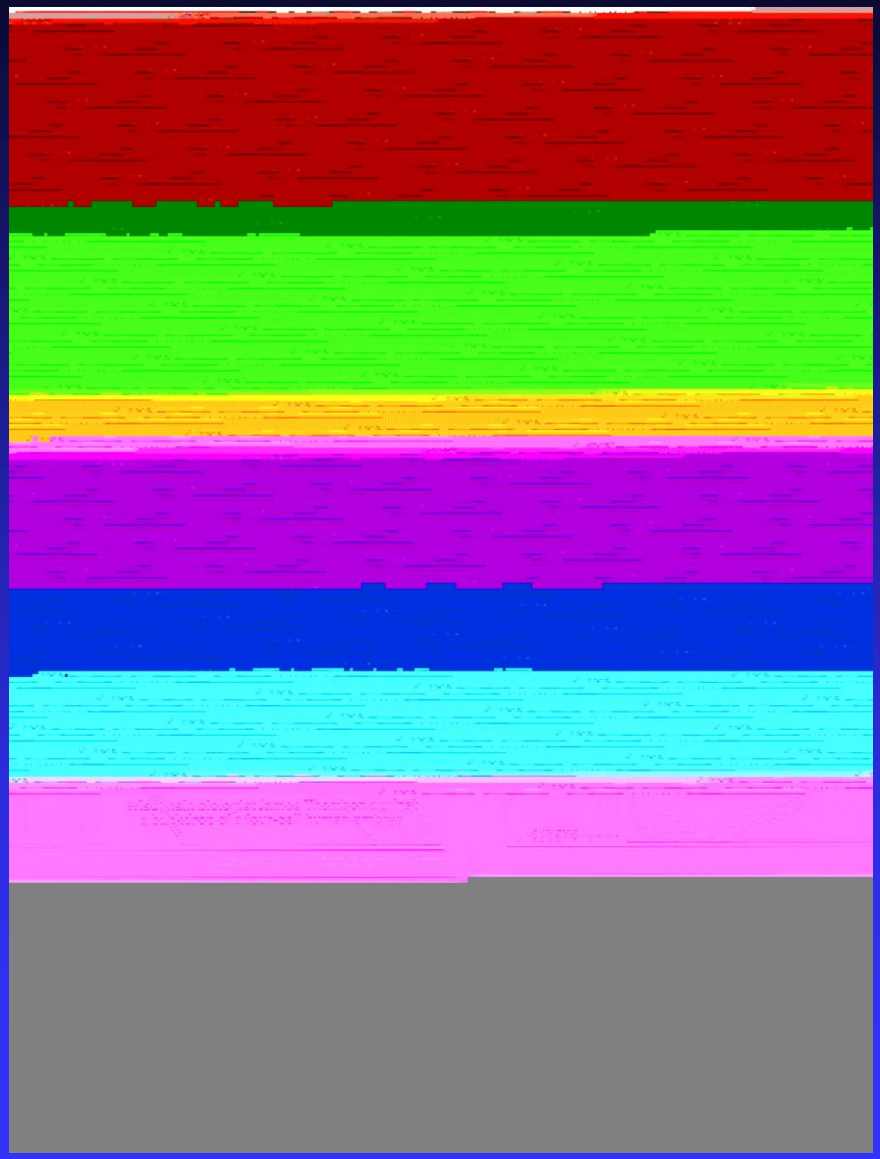
- AS cells found in small amounts throughout body
- ES cells are pluripotent
- Most AS cells appear to be multipotent

History of Human Embryonic Stem Cell Research



- In 1998, James Thomson (University of Wisconsin-Madison) isolated cells from the inner cell mass of the early embryo, and developed the first human embryonic stem cell lines.
- In 1998, John Gearhart (Johns Hopkins University) derived human embryonic germ cells from fetal gonadal tissue (primordial germ cells).
- Pluripotent stem cell “lines” were developed from both sources



In late 1998, James Thompson at UW-Madison discovered how to isolate and culture hES cells.

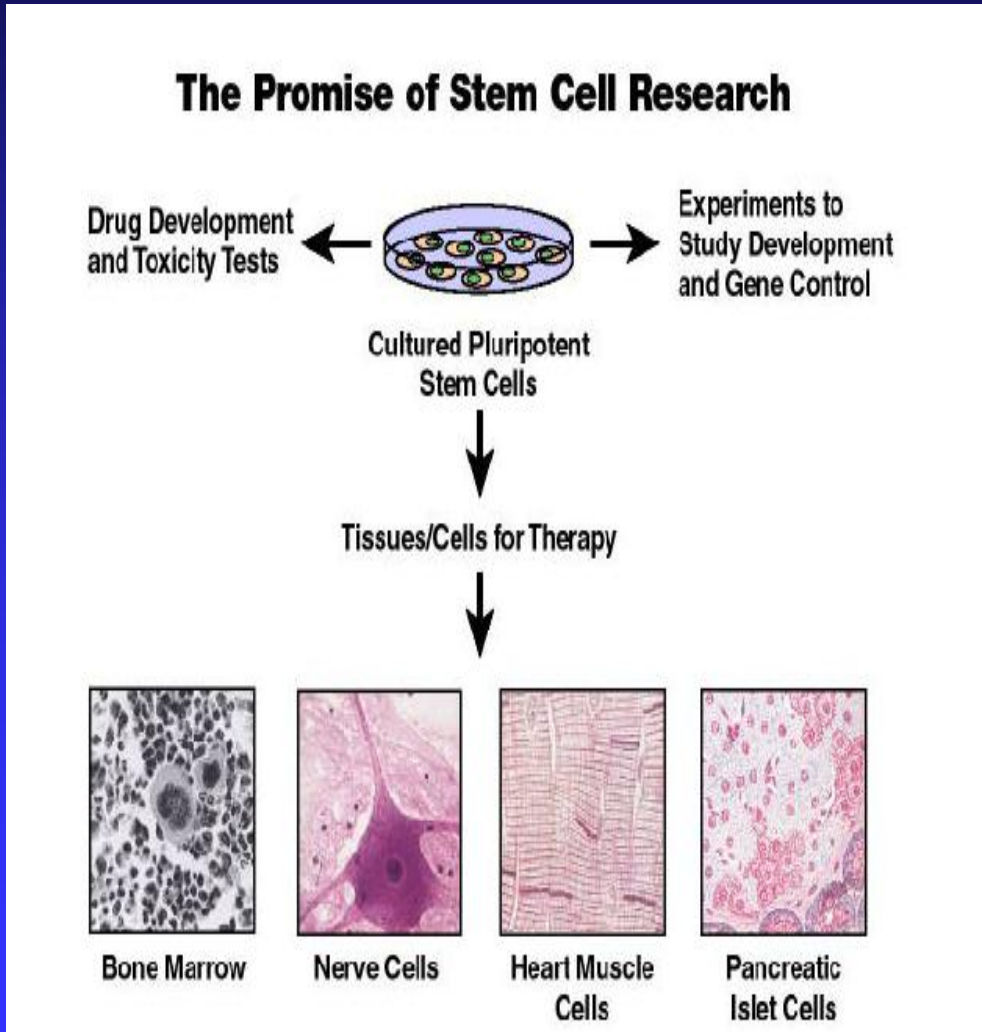
Why Are Embryonic Stem Cells Important?

- Embryonic stem cells are the interest of modern medicine.
- They have the ability to develop to virtually any other cell made by the human body.
- Drugs can be screened by testing them on human embryonic stem cells. This can reduce many drug related birth defects in the future.
- “Cell therapies”

Potential Clinical Uses

- Identify teratogens
- Drug toxicity tests

- Regenerative medicine
- Heart disease
- Islet cells for diabetes
- Neural cells
- Immunodeficiency



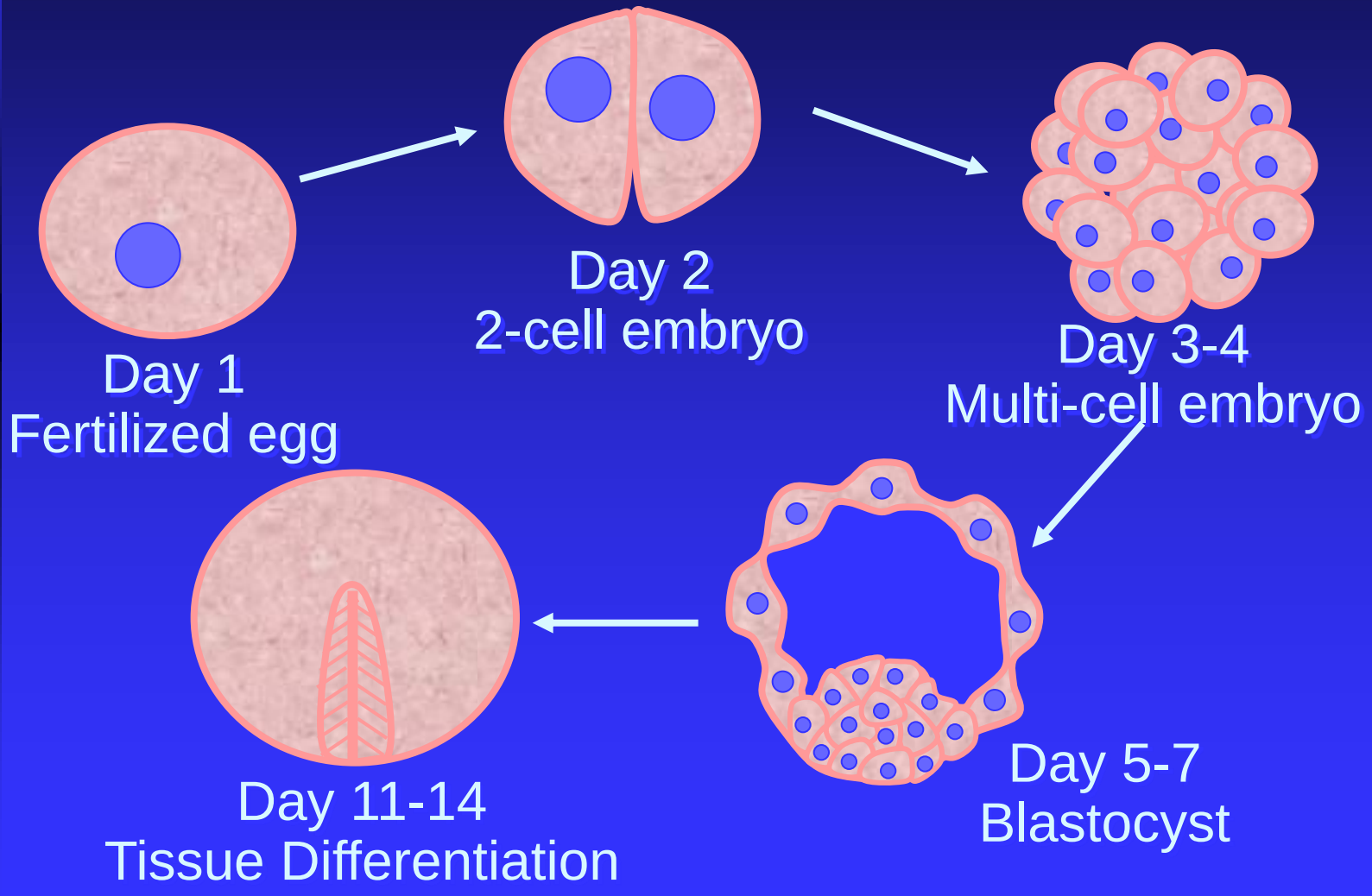
Why Don't We Take Stem Cells From Adults?

- This will not work because an adult cell has already reached its potential to regenerate.
- Adults don't have stem cells in many vital organs.
- When a tissue is damaged only scar tissue will develop.
- Adult stem cells cannot be cultured for long periods of time in vitro.

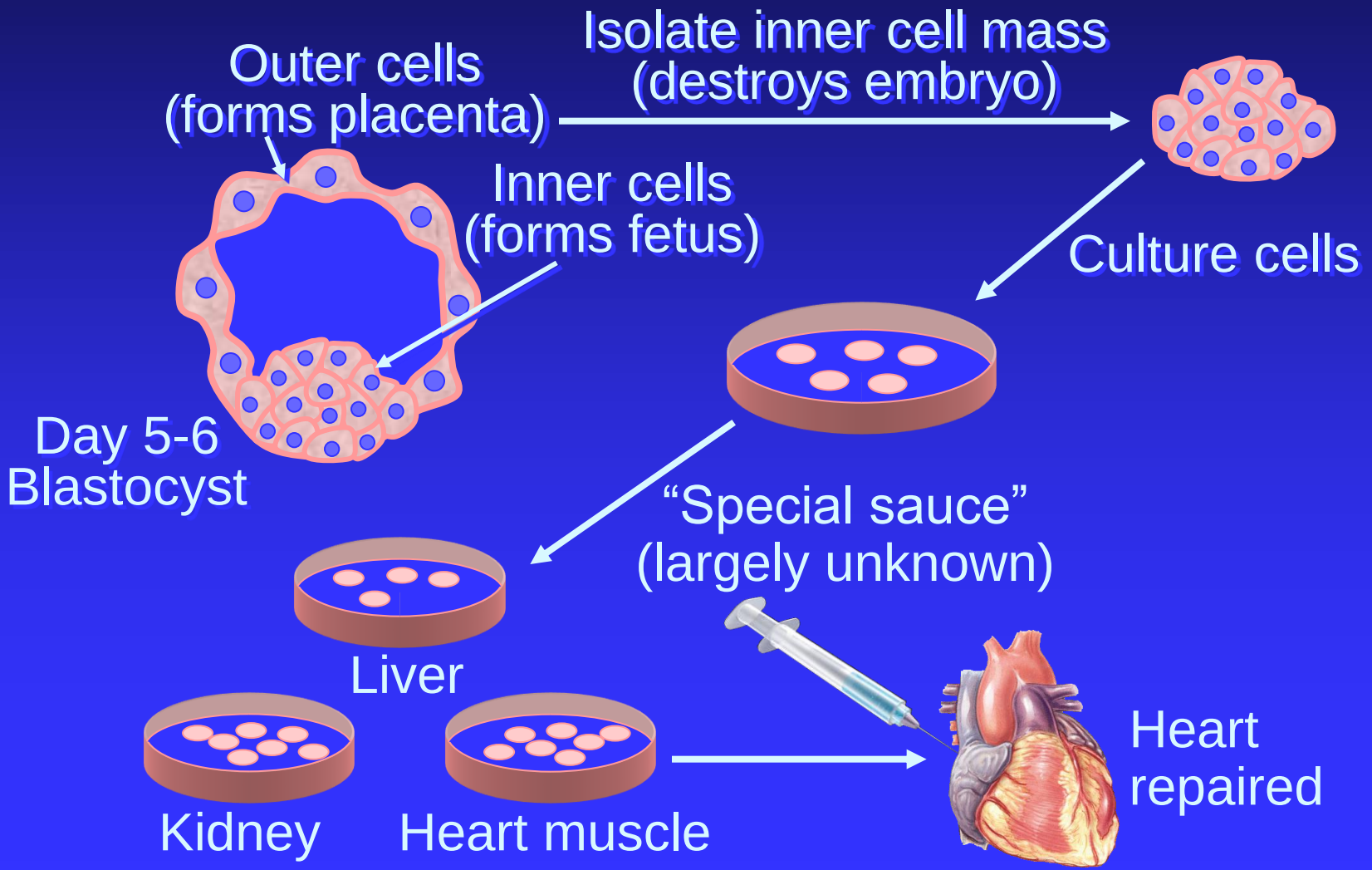
Sources of Embryonic Stem Cells

- Embryonic stem cell lines

Derivation and Use of Embryonic Stem Cell Lines

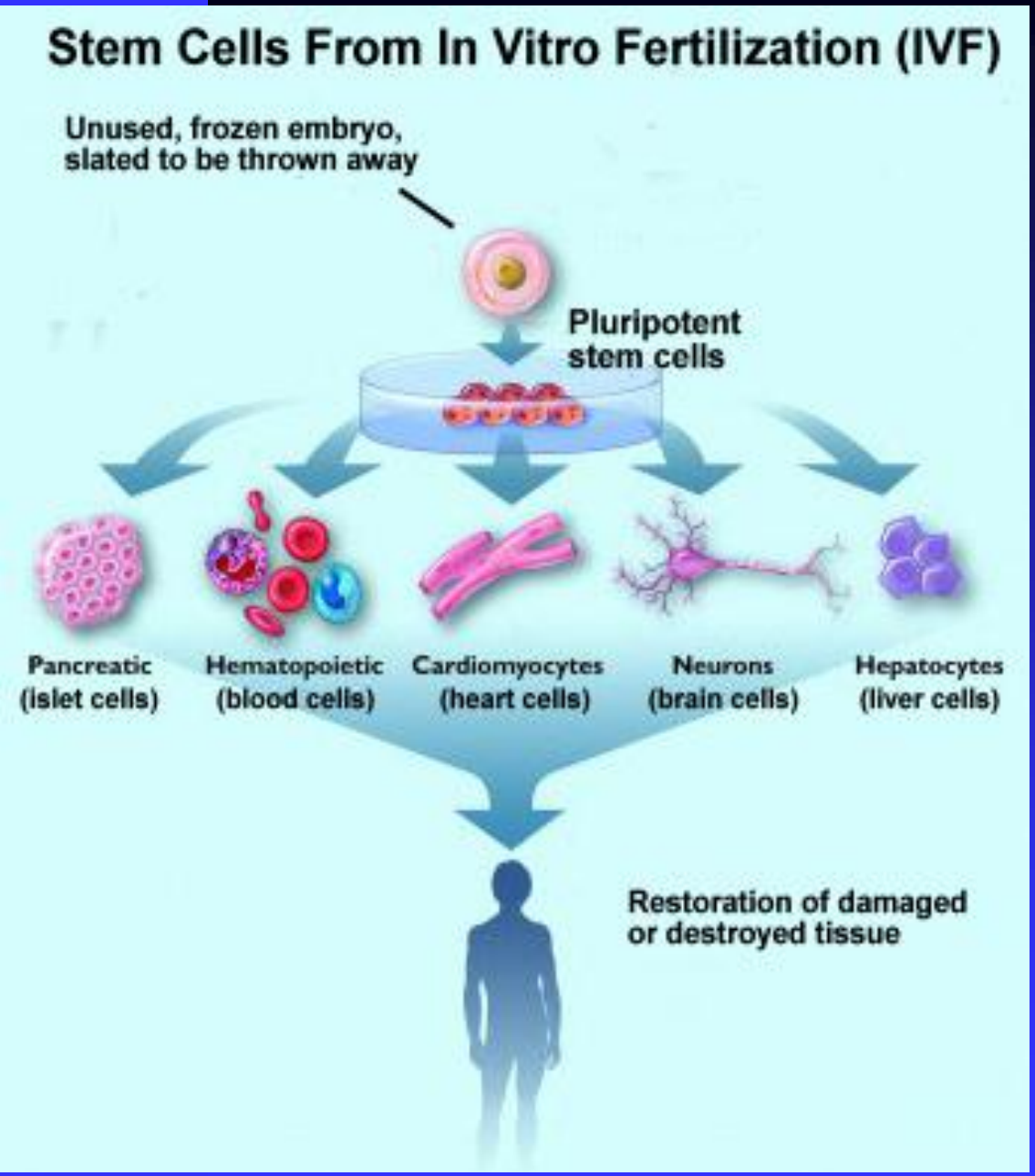


Derivation and Use of Embryonic Stem Cell Lines



Sources of Embryonic Stem Cells

- Embryonic stem cell lines
- Excess embryos from IVF clinics

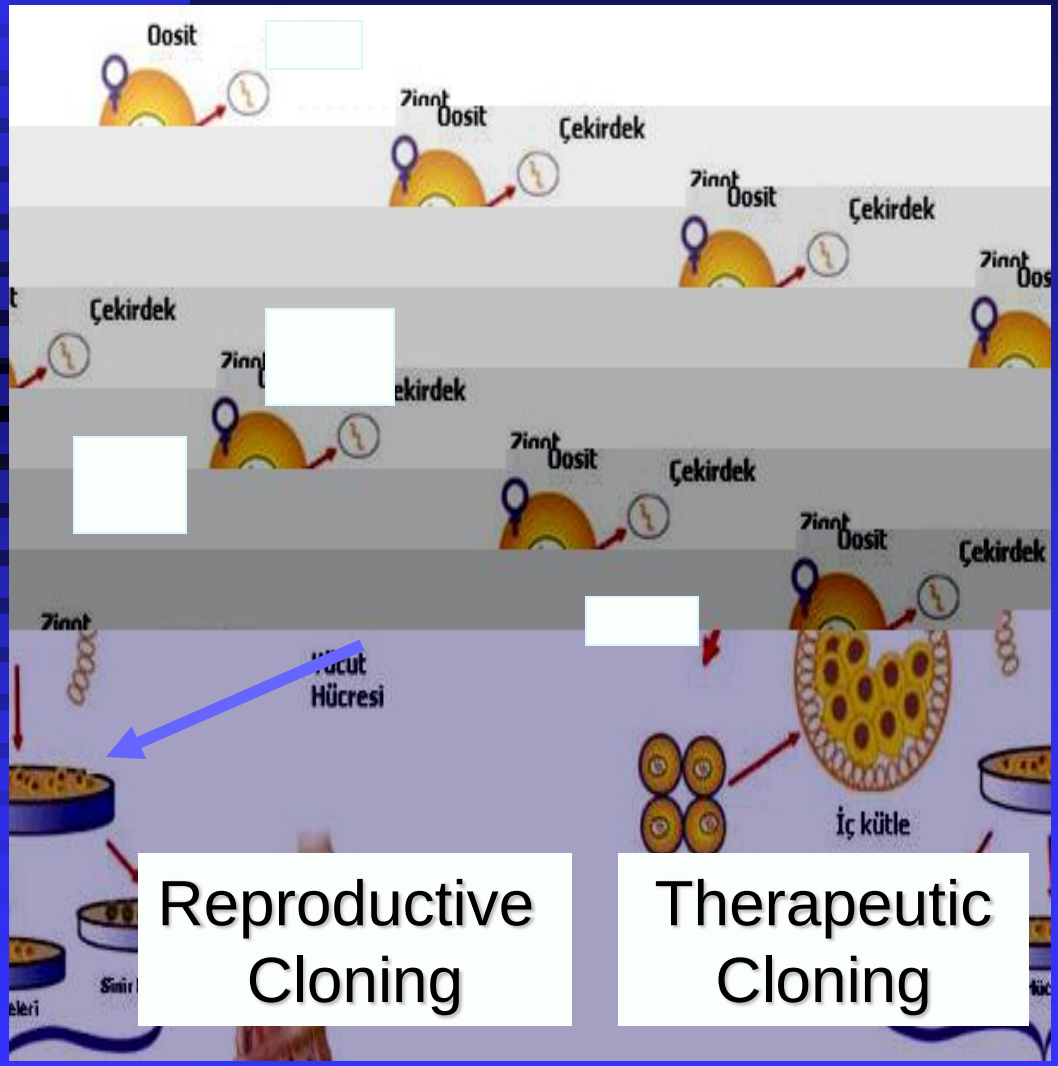


- Tens of thousands of frozen embryos are routinely destroyed when couples finish their treatment.
- These surplus embryos can be used to produce stem cells.
- Regenerative medical research aims to develop these cells into new, healthy tissue to heal severe illnesses.

Sources of Embryonic Stem Cells

- Embryonic stem cell lines
- Excess embryos from IVF clinics
- Embryos created for research by IVF
- Therapeutic cloning

Somatic Cell Nuclear Transfer (SCNT)



The nucleus of a donated egg is removed and replaced with the nucleus of a mature, "somatic cell" (a skin cell, for example).

The two cells are fused.

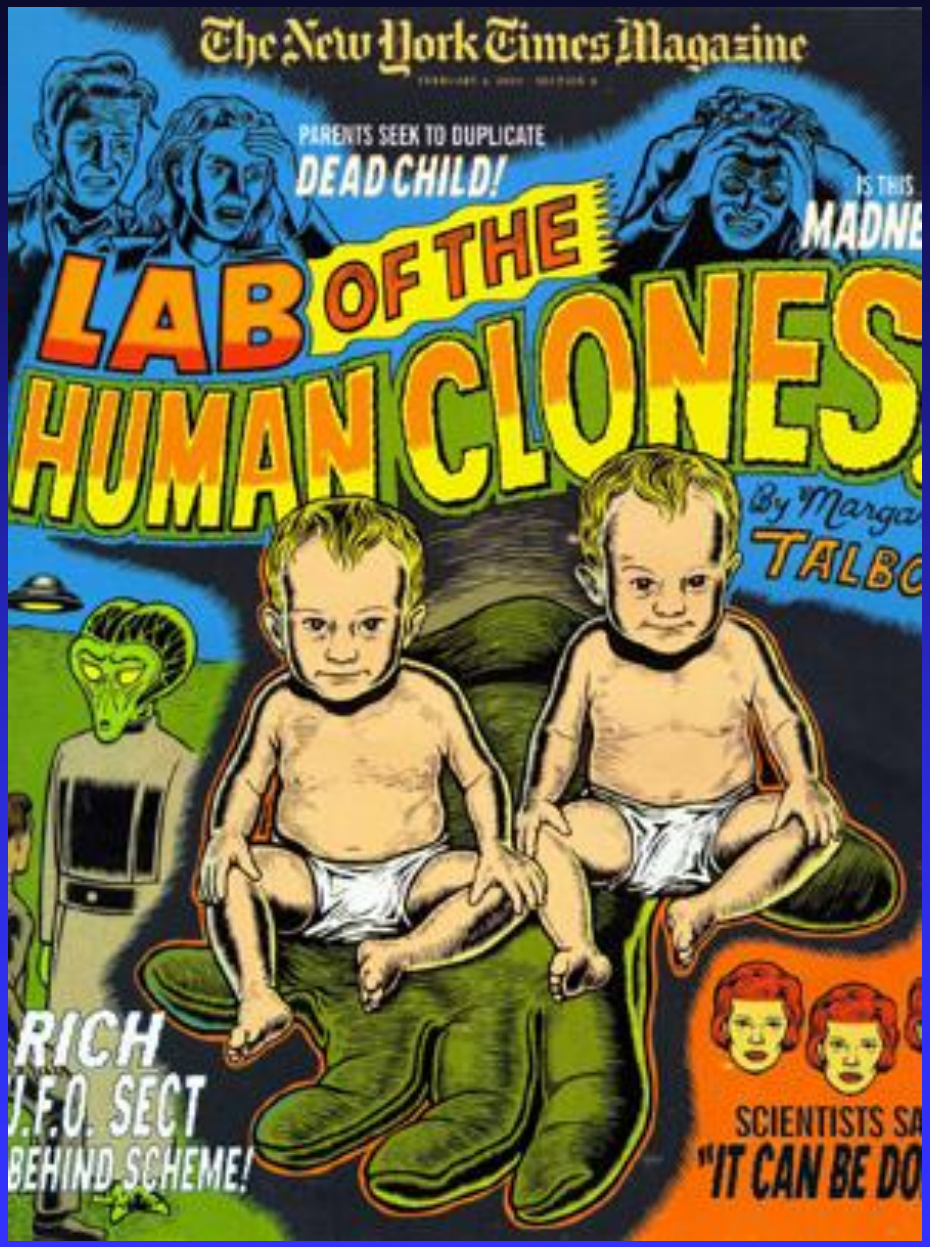
The resulting cell has the full potential (totipotent) to be an entire new organism.

The resulting stem cells can potentially develop into specialized cells that are useful for treating severe illnesses.

History of Somatic Cell Nuclear Transfer (Cloning)

- 1952 – Briggs and King cloned tadpoles
- 1996 – The first mammal cloned from adult cells was Dolly, the sheep.

- 1998 – Mice cloned
- 1998 – Cows cloned
- 2000 – Pigs cloned


The New York Times Magazine
PARENTS SEEK TO DUPLICATE
DEAD CHILD!
IS THIS
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LAB OF THE
HUMAN CLONES
By Marga
TALBO
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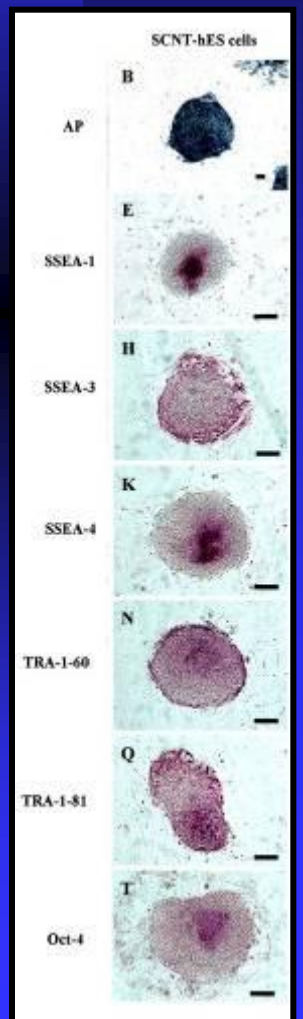
BEHIND SCHEME!
SCIENTISTS SA
"IT CAN BE DO

Early Successes – Human Cloning



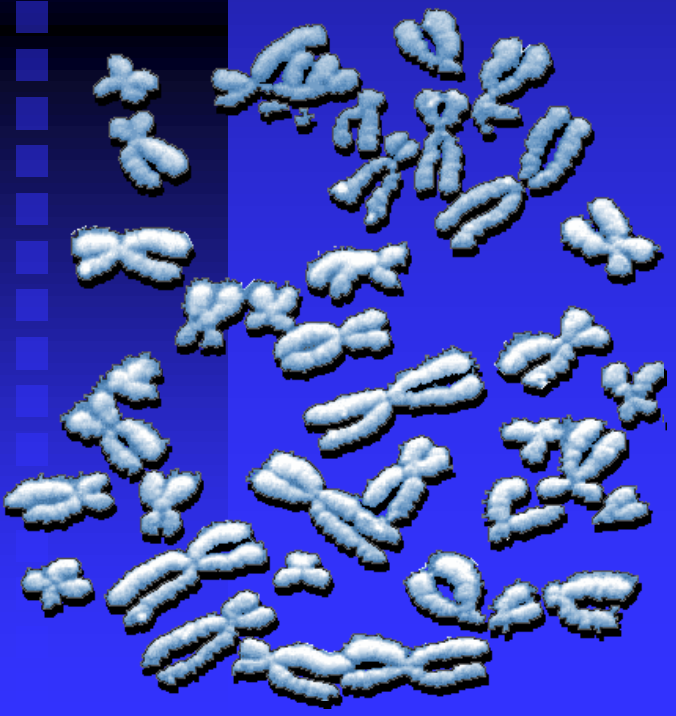
- 2001 – First cloned human embryos (only to six cell stage) created by Advanced Cell Technology (USA)
- 2004* – Claim of first human cloned blastocyst created and a cell line established (Korea) – later proved to be fraudulent

***Hwang, W.S., et al. 2004. Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst. *Science* 303: 1669-1674.**

Stem Cell Biology

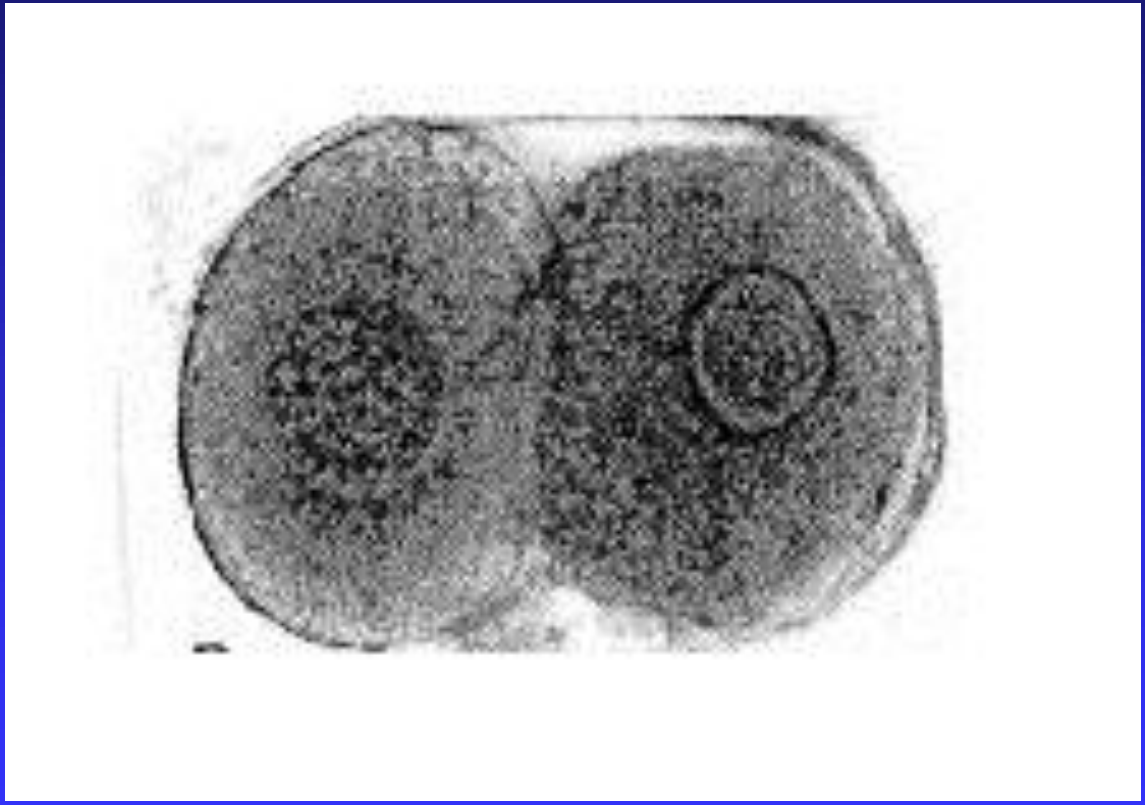
Does therapeutic cloning lead to the cloning of human beings?

Challenges to Stem Cell/Cloning Research

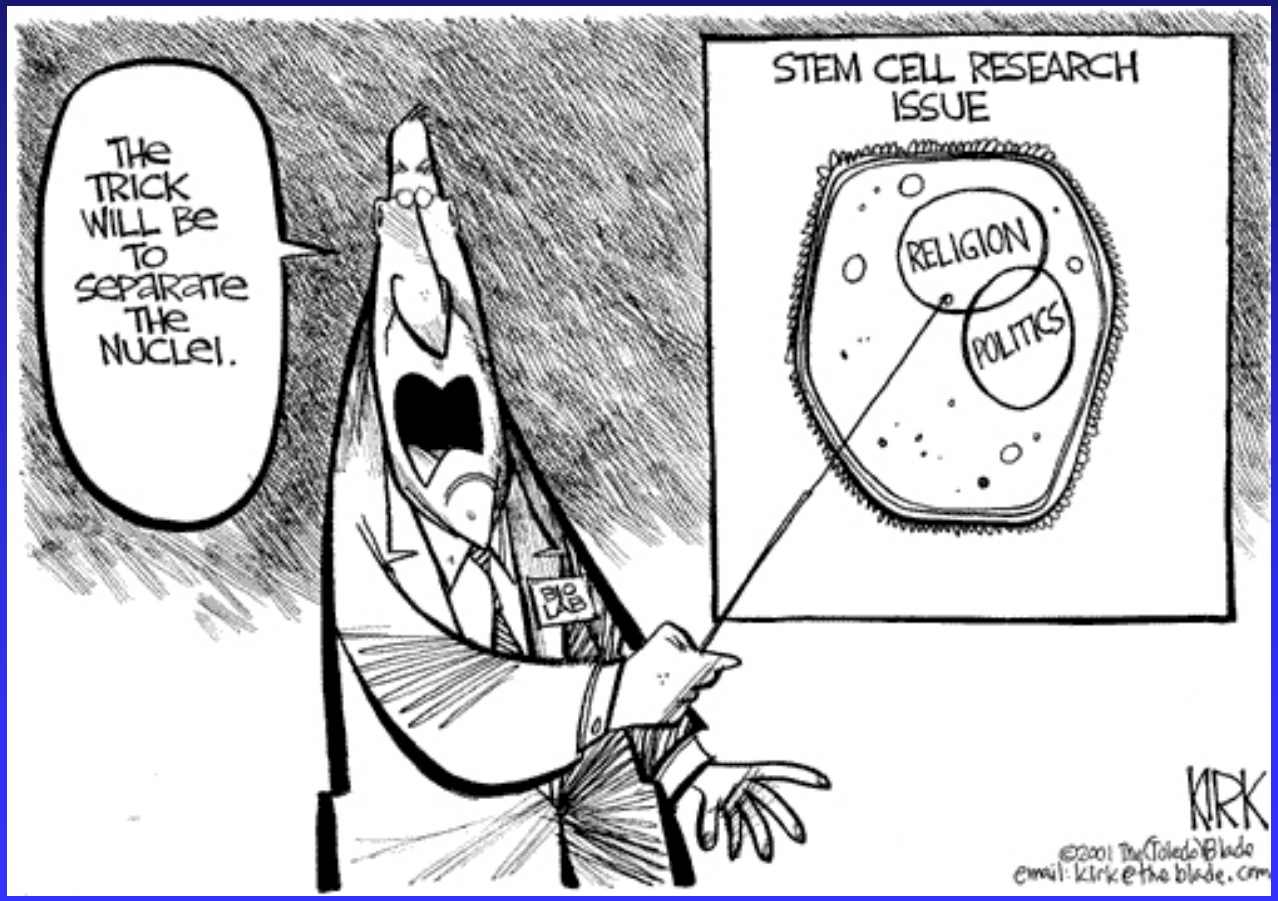


- Stem cells need to be differentiated to the appropriate cell type(s) *before* they can be used clinically.
- Recently, abnormalities in chromosome number and structure were found in three human ESC lines.

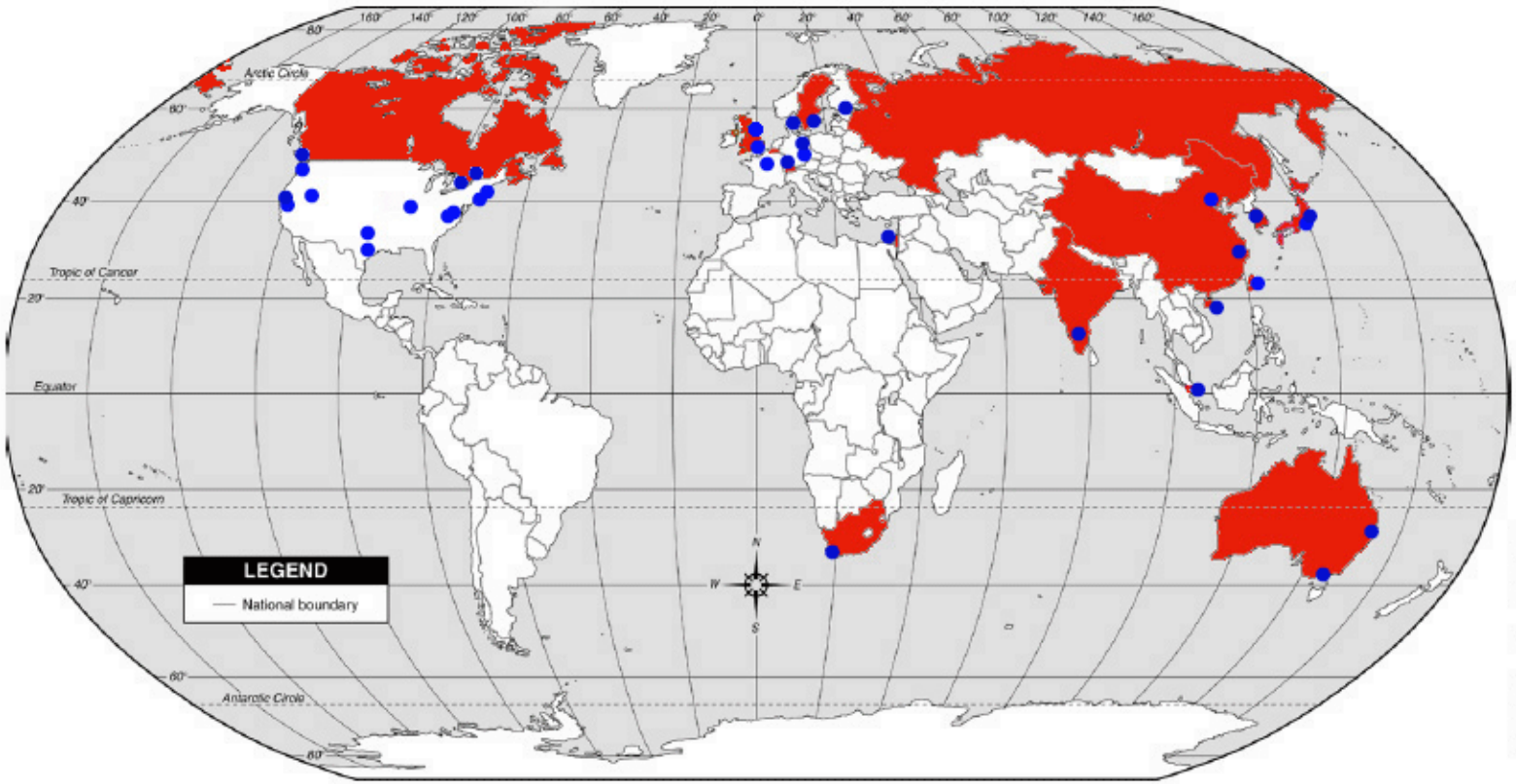
We start with this. . .



. . .and end with this:



Stem Cell Research Worldwide



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Countries with a permissive or flexible policy on embryonic stem cell research (in red)

- Denotes Genome Sequencing Center

Ethical debate

- Harvesting ES cells destroys the blastocyst also embryo
- If the embryo is a human, then it has a right to life
- “This is murder”
- ES cell research requires human cells
- Could create a commercial market for human cells
- “This devalues life”
- Keep in mind the embryos were not made for research purposes.

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When is it human?

- At what point does this entity become a human being with a right to life?
  - The point of conception
  - The point of implantation
- Early candidates for such morally significant points of demarcation include:
  - the initial appearance of the primitive streak (19 days),
  - the beginning of the heartbeat (23 days),
  - the development of the brain waves (48 days),
  - the point at which essential internal and external structures are complete (56 days) and
  - the point at which the fetus begins to move around (12-13 weeks).

Sources of stem cells

- Adult Stem Cells
- Embryonic Stem Cells
- Embryonic Germ Cells
- Induced Pluripotent Stem Cells

Induced Pluripotent Stem Cells (iPS)

- iPS are a type of pluripotent stem cell artificially derived from a non-pluripotent cell,

  i.e. an adult skin cell.
- iPS were first produced in 2006 from mouse cells and in 2007 from human cells.
- iPS are not totipotent and do not involve the destruction of an embryo.

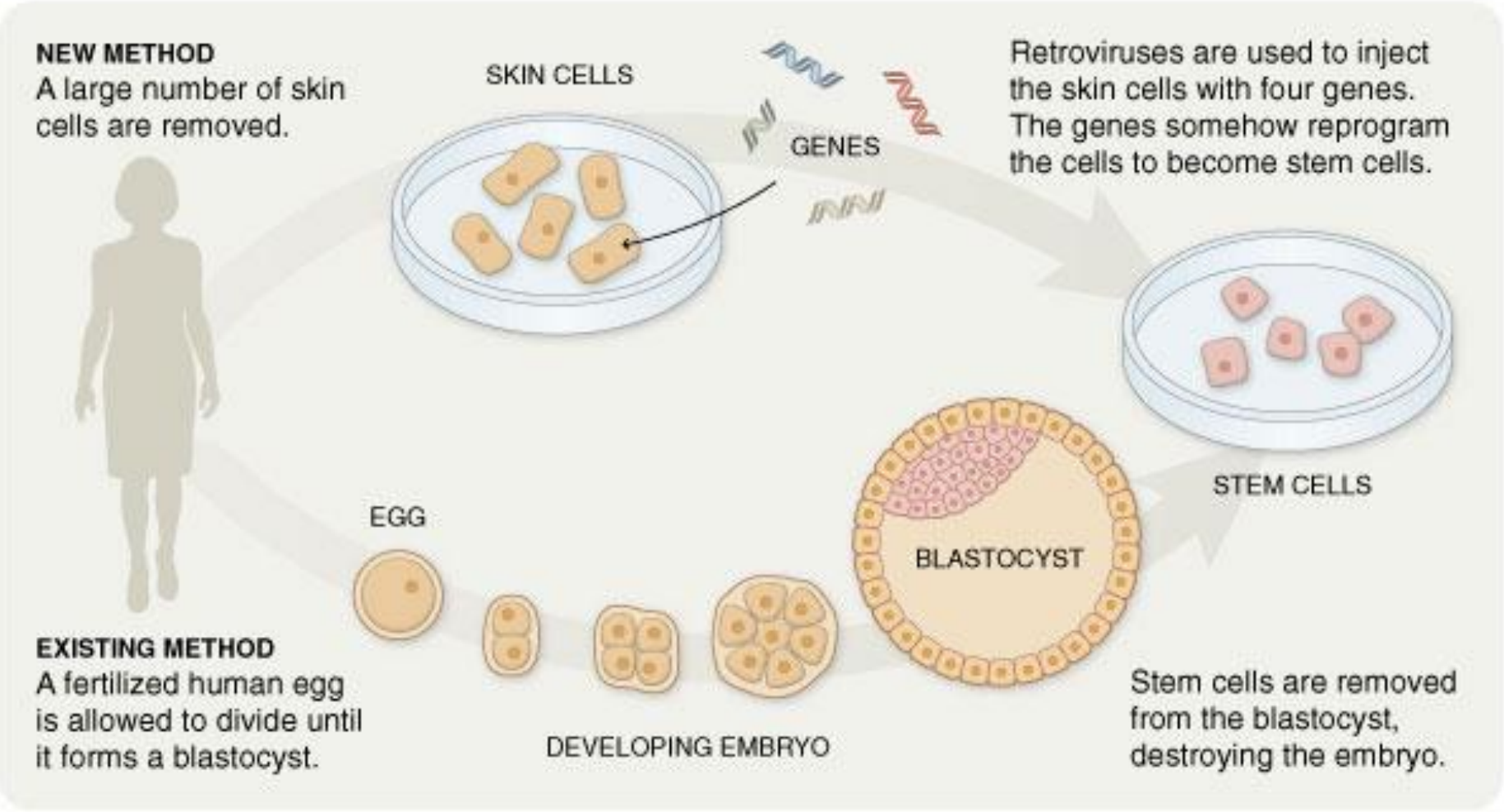
Induced Pluripotent Stem Cells (iPS)

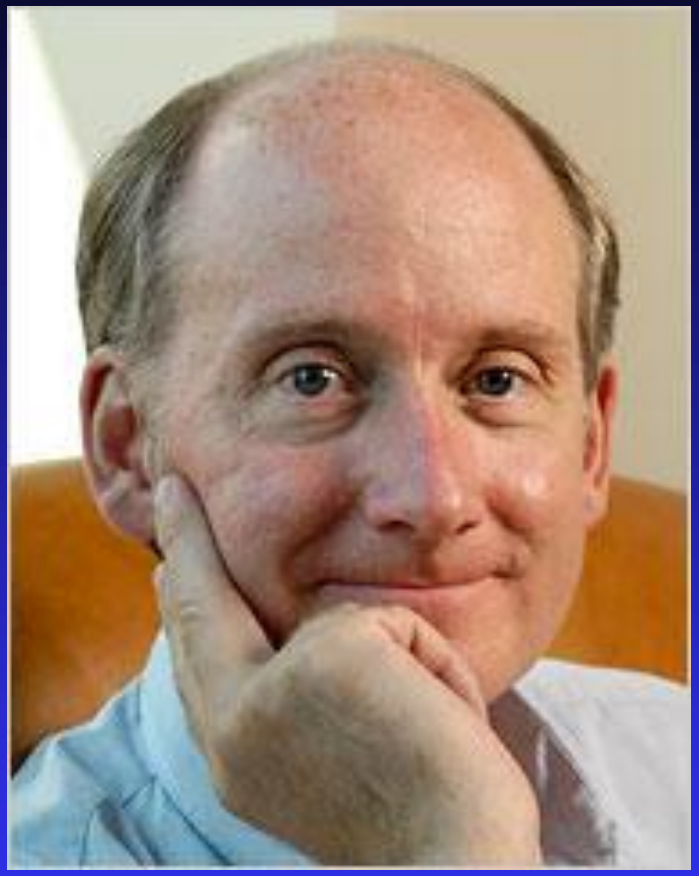
- Master regulator genes (turn other genes on or off)

- Retroviruses can slip other genes into the chromosomes.

Reprogramming Human Skin Cells

Researchers have developed a technique for creating stem cells without the controversial use of human eggs or embryos. If the method can be perfected, it could quell the ethical debate troubling the field.





James Thomson

Shinya Yamanaka

Thank you